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Mr. Stephen Johnson, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building, 1101 -A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Public Comments on the HPV Challenge Program Test Plan for Zinc 2-ethylhexanoate (Zn EHA, CAS Number 136-53-8) by Members of the Metal Carboxylates Coalition (Akcros Chemical Company, Baerlocher USA, Inc., Chemtura Corporation, Ferro Corporation, OM Group and The Shepherd Chemical Company).

The following comments on the HPV Challenge Program test plan for zinc 2-ethylhexanoate by members of the Metal Carboxylates Coalition (Akcros Chemical Company, Baerlocher USA, Inc., Chemtura Corporation, Ferro Corporation, OM Group and The Shepherd Chemical Company) are submitted on behalf of People for the Ethical Treatment of Animals, the Physicians Committee for Responsible Medicine, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

In our August 15, 2006 submission, we requested that EPA reopen the comment period for the metal carboxylates test plans, since, as a result of breaking up the category, the numbers of animals to be used has greatly increased and there are a number of serious scientific and animal welfare concerns that need to be addressed. This is the sixth set of comments that we have submitted on the new individual test plans.

The sponsoring companies propose to conduct a 7-day repeat dose oral test in rats and an acute fish toxicity test. If conducted, the acute fish toxicity test will cause the suffering and death of approximately 120 animals. Since we are unaware of any OECD guidelines for a 7-day repeat dose test, none are specified in the test plan, and no 7-day test is parts of the SIDS protocols on which the HPV program is based, we are unable to estimate the number of animals such a test would consume.

This test plan violates the principles of the October 1999 agreement among the EPA, industry, and health, animal protection, and environmental organizations, as well as the December 2000 *Federal Register* notice reconfirming that agreement which directed HPV Challenge Program participants to maximize the use of existing and scientifically adequate data to minimize further testing.

Zinc 2-ethylhexanoate is used as a catalyst for polyurethane foams and for unsaturated polyester resin systems. It is also used in liquid stabilizer formulations that allow flexible PVC to be processed. The sponsoring companies note that metal carboxylates readily dissociate into free metal and free acid. The proportion of dissociated salt is dependent on the pH, and the dissociation constant (pKa) is the pH at which 50% dissociation occurs. The pKa value for Zn EHA is reported to be 6.99 as determined in studies conducted by the Metal Carboxylates Coalition. These values indicate that complete dissociation will occur at the physiologically relevant pH of the mammalian stomach (pH 1.2). The sponsoring companies conclude therefore, that when administered orally, the toxicity of Zn EHA is due to the independent action of 2-ethyl hexanoic acid (2-EHA) and the free zinc ion. As a result, mammalian toxicity data for 2-EHA and the free zinc ion, or its simple metal salts, can serve as surrogate data for Zn EHA.

A 7-day repeat dose oral test in rats is proposed for zinc 2-ethylhexanoate. Existing data is summarized for repeated dose, reproductive and developmental toxicity endpoints for zinc salts and 2-ethyl hexanoic acid. The theoretical discussion of metal carboxylates dissociation presented in the test plan and summarized above clearly shows, and the sponsoring companies affirm, that data for zinc salts and 2-EHA can serve as surrogate data for Zn EHA. The only justification offered for proposing this duplicative test is to "provide empirical support for this characterization". In its comments on the Aluminum Stearates Category test plan, EPA specifically rejects this approach of conducting 7-day repeat dose studies on the metal carboxylate in order to confirm existing data for its dissociation products, noting that "it is not clear how the proposed 7-day repeated-dose bridging study would demonstrate that the dissociation products data are representative of aluminum stearates toxicity". EPA's comments also stress that EPA "does not support further testing for mammalian toxicity endpoints." Further, we are unaware of any OECD guideline for a 7-day repeat dose test and none is specified in the test plan. We strongly object to the proposal of this non-standard, unspecified test and urge EPA to again reject it along with any further testing for mammalian toxicity endpoints.

Because the Metal Carboxylates Coalition submitted its original test plan in 2003, it may be unaware that a similar approach, using existing data on dissociation products, was subsequently endorsed by the EPA and all stakeholders in 2004 for E. I. du Pont de Nemours & Company's test plan for triisopropylborate, a compound which breaks down to isopropanol and boric acid in water (see http://www.epa.gov/oppt/chemrtk/triprobt/c14841tc.htm). This approach has been used in a number of other test plans as well in which compounds dissociate at low pH and the toxicity data on the dissociation products has been used to meet the SIDS requirements.

An acute fish acute toxicity test is also proposed for zinc 2-ethylhexanoate. Reliable existing data is summarized for ecotoxicity endpoints in fish, daphnia and algae for zinc chloride and 2-ethyl hexanoic acid. As with the 7 day repeat dose test, the sponsoring companies affirm that since Zn EHA dissociates at environmental pH, the data for the dissociation products can be used to represent its aquatic toxicity. Once again, the only justification offered for proposing this duplicative test is to provide empirical support for this characterization. We urge EPA to reject this test which the sponsoring companies themselves convincingly argue is unnecessary. In addition, no reliable ecotoxicity data for aquatic plants or invertebrates exist for Zn EHA. The fish test is intended to show whether exposure to Zn EHA will result in large-scale fish death

thereby predicting economic loss and ecologic damage. If this exposure kills the food on which fish subsist, it could deplete fish populations even without direct fish toxicity. Since the toxicity of Zn EHA to aquatic plants and invertebrates is still unknown, a test on fish is premature. Finally, the applicability of ECOSAR and non-animal ecotoxicity tests, such as the DarT test[1] and TETRATOX test[2] should be considered. If a fish acute toxicity test is still perceived to be required, ECVAM's Ecotoxicology Task Force recently published an evaluation of a fish acute threshold (step-down) test concept with the potential to reduce the number of fish used in ecotoxicity testing by 53.6%-71.2%.[3]

In summary, we strongly object to the proposed 7-day repeat dose oral study in rats in order to provide empirical support for the characterization that data for zinc salts and 2-EHA can serve as surrogate data for Zn EHA. We urge EPA to reject this test along with any further testing for mammalian toxicity endpoints as it has already done in its comments on the Aluminum Stearates Category test plan. We also urge EPA to apply similar reasoning in its consideration of the proposed acute fish toxicity test and to reject it as well. At a minimum, the applicability of the suggested alternatives to this test should be considered.

Sincerely,

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Research & Investigations

[1] Nagel, R. 2002. DarT: the embryo test with the zebrafish *Danio rerio*: A general model in ecotoxicology and toxicology. *ALTEX* 19 (Suppl. 1), 38-48.
[2] Schultz, T.W. 1997. TETRATOX *Tetrahymena pyriformis* population growth impairment endpoint: A surrogate for fish lethality. *Toxicological Methods* 7, 289-309.
[3] Jerama, S., et al. 2005. A strategy to reduce the use of fish in acute ecotoxicity testing of new chemical substances notified in the European Union. *Regulatory Toxicology and Pharmacology* 42, 218–224.